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Patterns and Prevalence of Metabolic Syndrome among Persons Receiving Treatment with Antipsychotic Medications

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ABSTRACT PAGE

The treatment of schizophrenia is heavily reliant on financial, health, and social care. Despite the low occurrence of schizophrenia in the population, the total health care costs of schizophrenia are similar to more prevalent mental disorders. Therefore, resources need to be directed at finding and implementing the most effective and least costly treatment regimes. The current study examined differences in weight, lipid and glucose levels, and metabolic irregularities between schizophrenic patients receiving first and second generation antipsychotics. Results indicated that there was a higher prevalence of metabolic disorder among patients treated with second generation antipsychotics (SGAs) than those treated with first generation antipsychotics (FGAs). Patients receiving SGAs also displayed greater increases in weight and systolic blood pressure from first to last assessment than those being treated with FGAs. Second generation antipsychotics were not superior on measures of clinical efficacy than first generation antipsychotics. In combination, these findings suggest that the benefits of SGAs may not outweigh the side effects and financial cost of this class of antipsychotics.

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To my family and Kori for all their patience and support

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Patterns and Prevalence of Metabolic Syndrome Among Persons Receiving Treatment with Antipsychotic Medications

Schizophrenia is a chronic, deteriorating brain disorder that involves many brain and neurochemical abnormalities (Andreasen, 1997; Cahn et al., 2002). Patients with schizophrenia evidence psychological, social, cognitive, and occupational deficits (Burton, 2006). Compared to the general population, attention/vigilance, working memory, verbal and visual learning and memory, reasoning and problem solving, processing speed, and social cognition are disturbed in schizophrenics (Ikebuchi, Nakagome, & Takahashi, 1999).

Negative symptoms of schizophrenia are often characterized as "deficient symptoms" because they reflect deficiencies in normal behavior (Shean, 2004). Negative symptoms include: disorganized speech, grossly disorganized or catatonic behavior, affective blunting, poverty of speech (alogia), decreased level of activity (avolition), decreased pleasure (anhedonia), and poor executive functioning and self care skills (American Psychiatric Association [APA], 2000; Worrel, Marken, Beckman, & Ruehter, 2000). Positive symptoms represent an excess in normal behaviors (Toomey, Seidman, Lyons, Faraone, & Tsuang, 1999). These symptoms include disorganized thinking, hallucinations, and delusions.

Costs of Schizophrenia

Approximately 1% of the population is afflicted with schizophrenia (National Institute of Mental Health [NIMH], 2005). Despite schizophrenia's low prevalence, its costs are similar to more widespread mental illnesses such anxiety disorders (Rice, 1999). In 2002, the economic burden of schizophrenia was approximately $62.7 billion (Wu et

al., 2005). Included in the overall health care costs of schizophrenia are direct costs (e.g., drug and hospitalization costs) and indirect costs (e.g., loss of productivity: unemployment, loss of income, and premature death from suicide).

The estimated relapse rate of schizophrenia is as high as 3.5% per month (Csernansky & Schuchart, 2002). A minority of schizophrenic patients, approximately 25% (Bleuer, 1978), fully recover. The remaining percentage of schizophrenics either remain in a state of severe psychosis (10%) or experience acute relapses (65%). Cognitive deficits affecting memory, social skills, and attention can impede a schizophrenic's ability to live independently (Velligan et al., 1997) and fulfill social roles (Gerlach, 2002). These deficits combined with a high incidence of relapse lead to long and/or frequent and expensive hospital stays. The estimated annual cost of hospitalizations to relapse among individuals with schizophrenia is $2 billion.

Schizophrenic patients occupy 8.8% of all hospital beds, 11.4% of all nursing home beds, and 40.3% of all mental health facility beds (Worrel et al., 2000). Individuals who are discharged may still require ongoing and costly outpatient care. Therefore, the high economic costs of relapses and re-hospitalizations associated with schizophrenia contribute to the high overall health care costs of this disorder.

Comorbidity and Cost

Individuals with schizophrenia often suffer from chronic physical illness (Marder et al., 2004). Many medical problems arise due to poor nutrition and hygiene, tobacco usage, inadequate treatment, and serious problems associated with side effects of antipsychotic medications (Goldman, 1999; Marder et al., 2004; NIMH, 2005; Shean, 2004). Carney, Jones, and Woolson (2006) found that schizophrenic patients have more

comorbid medical conditions than those without the disorder. Furthermore, over 33% of persons with schizophrenia had three or more comorbid disorders (Carney et al., 2006). Carney et al. (2006) found that individuals with schizophrenia have more months of follow up and more non-mental health care visits than those without schizophrenia. Compared with the general population, individuals with schizophrenia are more likely to have respiratory illness even after controlling for the effects of smoking (Sokal et al., 2004). Current medical problems may exacerbate the psychosis and depression associated with schizophrenia (Dixon, Postrado, Delahanty, Fischer, & Lehman, 1999), thus making patients more difficult and expensive to treat. The high prevalence of chronic medical conditions among individuals with schizophrenia also contributes to increased mortality (Brown, 1997).

Results from the Epidemiologic Catchment Area (ECA) Study indicate that approximately 47% of individuals with a lifetime diagnosis of schizophrenia or schizophreniform disorder also meet the diagnostic criteria for substance abuse. Individuals with schizophrenia are 4.6 times more likely of having a substance abuse disorder than those without the disorder (Regier et al., 1990). The high prevalence of substance abuse and medical problems among schizophrenic patients indicates that the cost of care for schizophrenia may be much higher than initial estimates may suggest. These indirect costs of schizophrenia may contribute to the large proportion of national health care expenditure on schizophrenia worldwide (Beard, Maciver, Clouth, & Rüther, 2006).

Psychopharmacology of Schizophrenia

Neurodevelopmental deficits contribute to some of the cognitive and attentional impairments evident in schizophrenics even before the onset of overt psychoses. Consequently, these impairments may contribute to a schizophrenic's capacity to be rehabilitated (Kotrla & Weinberger, 1995; Smith, Hull, Romanelli, Fertuck, & Weiss, 1999). Although the course of schizophrenia varies, patient outcomes are largely determined by medication (Shean, 2004). The American Psychological Association (1997) has determined that antipsychotics can lead to a reduction in the relapse rate for individuals with schizophrenia. Therefore, long-term psychopharmacological treatment may be necessary for improved disease outcomes.

Studies have identified several anatomical abnormalities in the brains of schizophrenic patients. However, researchers believe that the symptoms of schizophrenia result from circulatory dysfunction rather than localized brain areas (Wiser et al., 1998). Some of the biochemical systems that have been implicated in schizophrenia include the dopaminergic, glutamate, and the GABA systems (Javitt & Laruelle, 2006).

Dopamine Hypothesis

The dopamine hypothesis is one of the longest lasting and most influential explanatory models of schizophrenia (Kapur & Mamo, 2003). According to this hypothesis, schizophrenia arises as a result of an excess of the neurotransmitter dopamine (DA) in the brain, which is responsible for the positive symptoms characteristic of schizophrenia. After the introduction of chlorpromazine in 1952 and other first generation antipsychotics (FGAs) shortly after, researchers discovered that the biological mechanism underlying schizophrenia involves D2 receptors, one of the two main families of DA

receptors. This finding was supported by the correlation between the clinical efficacy of FGAs and D2 receptor affinity (Horacek et al., 2006; Peroutka & Snyder, 1980). Therefore, researchers have historically believed that D2 receptors are the major site of action in schizophrenia. According to the dopamine hypothesis, a hyperfunction of DA transmission in the striatum accounts for the positive symptoms of schizophrenia. Antipsychotics work by antagonizing the D2 receptors, which reduces DA levels in the mesolimbic pathway.

First Generation Antipsychotics

Antipsychotics play a central role in the treatment of schizophrenia and other psychotic disorders. First generation antipsychotics were formulated to antagonize the D2 receptor. Research has shown that FGAs effectively reduced positive psychotic symptoms. However, FGAs may worsen the negative symptoms of schizophrenia by antagonizing DA in the mesocortical pathway where DA is underactive (Shean, 2004).

First generation antipsychotics range in their clinical potency from low to high. Low potency drugs include Thorazine (chlorpromazine), Mellaril (thioridazine), and Serentil (mesoridazine). Medium potency drugs include Loxatane (loxapine), Moban (molindone), and Trilafon (perphenazine). High potency drugs include Haldol (haloperidol), Prolixin (fluphenazine), Navane (thioxanthene), and Stelazine (trifluoperazine) (Worrel et al., 2000).

Extra-pyramidal side effects. First generation antipsychotics often produce extrapyramidal symptoms (EPS). Caesy (1998) estimated that up to 90% of patients on FGAs experience EPS. The nigrostriatal pathway is involved in the presence of EPS such as dystonia, akathisia, and concomitant movement disorders. Dopamine antagonism at

receptor sites in these pathways produces motor dysfunction and other symptoms bearing resemblance to Parkinson's disease (Weiden, 2007). According to the DSM-IV-TR, neuroleptic induced parkinsonism is "Parkinsonian tremor, muscular rigidity, or akinesia developing within a few weeks of starting or raising the dose of a neuroleptic medication (or after reducing a medication used to treat extrapyramidal symptoms)" (APA, 2000, p. 735). In order for EPS that affects motor functionality to arise, there needs to be an 80% loss of DA content in the striatal area of the basal ganglia (Weiden, 2007). According to a PET study, patients consistently report EPS when they are receiving neuroleptic drugs at doses that involve an occupancy rate of over 80% at the D2 receptor (Farde, Mack, Nyberg, & Halldin, 1997).

Due to the physical discomfort and social stigma associated with EPS, FGAs producing these side effects often lead to a lower quality of life (Strejilevich et al., 2005), poor treatment compliance (Buchanan, 1992), and increased mortality rates (Ballesteros, González-Pinto, & Bulbena, 2000). Patients with severe EPS also demonstrate impaired perception and cognitive functioning (Krausz, Moritz, Naber, Lambert, & Andresen, 1999). Because treatments for EPS often demonstrate minimal effectiveness (Soares & McGrath, 1999), EPS are often unavoidable and severe limitations of FGAs.

Other FGA side effects. Hyperprolactinemia is a common side effect of FGAs. By occupying D2 receptors, FGAs cause a disinhibition of plasma prolactin levels by blocking DA release (Ben-Jonathan & Hnasko, 2001). This inhibition of DA results in elevated prolactin levels. Hyperprolactinemia can cause sexual side effects such as irregular menstruation, lactation in women and men, and sexual dysfunction in men.

Most FGAs, chlorpromazine and thioridazine in particular, have anticholinergic actions (Crook, Tomaskovic-Crook, Coplov, & Dean, 2001). Administration of these neuroleptic drugs increases the activity of presynaptic receptors in the central and peripheral nervous symptoms that inhibit the release of acetylcholine (ACh), thus depleting Ach levels (Lacroix, Hows, Shah, Hagan, & Heidbreder, 2003; Snyder, Greenburg, & Yamamura, 1974). Depleted ACh levels lead to memory and learning impairments (Kasper & Resinger, 2003). Other anticholinergic effects include dry mouth, constipation, retention of urine, and blurred vision. The elderly are especially sensitive to the anticholinergic effects of FGAs. High-potency FGAs are less anticholinergic and less sedating than lower potency FGAs (Zhang & Bymaster, 1999). However, these high-potency agents are more likely to cause parkinsonism, akathesia, and dystonia (Mukherjee, 1982; Snyder et al., 1974; Tarsy & Baldessarini, 2006). Because many FGAs block DA transmission and have anticholinergic effects at muscarinic receptors (Crook et al., 2001), these neuroleptics are more likely to produce tardive dyskinesia than other neuroleptic drugs (Sayers, Burki, Ruch, & Asper, 1976).

Second Generation Antipsychotics

Second generation antipsychotics (SGAs) were introduced in the United States in late 1980s. In 1989, clozapine (Clozaril) was the first SGAs antipsychotic to be approved by the Food and Drug Administration (FDA). Other SGAs include: Risperdal (risperidone) Zyprexa (olanzapine), Seroquel (quetiapine), Geodon (ziprasidone), and Abilify (aripiprazole). Second generation antipsychotics are characterized by a higher 5-HT2/DA2 occupancy ratio than FGAs (Mamo et al., 2004). Studies have shown that SGAs effectively reduce positive (Bouchard et al., 2000) and negative symptoms

(Martyns-Yellowe, 1994), and the risk of relapse for schizophrenic patients without the traditional side effects associated with FGAs (Haro & Salvador-Carulla, 2006). Because SGAs demonstrate fewer and less severe EPS across all age groups (Correll, Leucht, & Kane., 2004; Weiden, 2007), SGAs may contribute to a higher quality of life and greater treatment compliance among schizophrenic patients than FGAs (Gerlach, 1999). Thus, some have argued that SGAs have the capacity to diminish the incidence of acute psychotic episodes that are responsible for frequent and long-lasting hospital stays. As a result, SGAs have become the preferred pharmacotherapy for schizophrenia (Correll et al., 2004).

Side effects of SGAs. In addition to the potential benefits of SGAs, this class of antipsychotics also has its own financial costs and medical risks. EPS is still a distressful and problematic side effect of many SGAs, especially in elderly populations. Research suggests that taking a high dose of some SGAs increases the risk of EPS (Correll et al., 2004; Kane, 2001). Therefore, EPS is still common among schizophrenic patients taking higher than recommended doses of SGAs such as clozapine, risperidone and olanzapine (Correll et al., 2004; Weiden, 2007).

One of the major limitations of SGAs is weight gain (Weiden, 2007). Weight gain associated with SGAs increases the risk of developing metabolic syndrome (MS). Research suggests that individuals whose weight increases by 5% are 200 times more likely to develop MS (Everson et al., 1998). Therefore, patients taking SGAs are more vulnerable to developing MS than individuals on FGAs.

The metabolic abnormalities associated with SGAs also increase the risk of developing MS. Diagnosis for MS is established when there is a co-occurrence of at least

three of the following conditions: elevated triglycerides, HDL cholesterol, blood pressure, fasting glucose levels, and abdominal obesity (Expert Panel on Detection, 2001). Metabolic syndrome elevates the risk for cardiovascular disease, which is one of the leading causes of morbidity and mortality among schizophrenic patients (Meyer, 2003). The insulin sensitivity and other metabolic abnormalities associated with MS often predict diabetic complications. Metabolic syndrome can exacerbate pre-existing diabetes mellitus or can significantly increase the risk of developing this condition (Newcomer et al., 2002). Compared to the general population, individuals with schizophrenia are twice as likely to be diagnosed with type 2 diabetes mellitus (Dixon et al., 2000).

The increased morbidity and mortality rates for many of the conditions associated with MS (e.g., obesity, diabetes mellitus, and cardiovascular disease) emphasize the public health implications of SGAs (Jin, Meyer, & Jeste, 2004). Weight gain associated with medication use often leads to treatment noncompliance (Baptista, 1999). Schizophrenics with poor treatment compliance relapse more frequently than those who comply with treatment. Therefore, weight gain associated with the use of SGAs may lead to poor treatment prognosis. Not all SGAs have the same side effect profiles. However, the potentially harmful side effects of SGAs and high medical costs associated with assessment and treatment of abnormalities in glucose and lipid metabolism (Nichols & Brown, 2005) may counter-balance the potential benefits associated with these drugs.

Current Study

The treatment of schizophrenia is heavily reliant on financial, health, and social care. Therefore, resources need to be directed at finding and implementing the most effective and least costly treatment regimes. Many patients and clinicians discontinue

antipsychotic treatments due to adverse side effects. Therefore, the goal of pharmacological treatments for schizophrenia is to maximize treatment effectiveness while limiting the number of side effects that lessen patients' quality of life. Because SGAs are associated with a reduced risk of EPS, researchers believed that the potential clinical benefits of SGAs outweighed the costs associated with these drugs. However, recent research has suggested that SGAs may not be superior to FGAs in terms of clinical efficacy (Geddes, Freemantle, Harrison, & Bebbington, 2000). Furthermore, the potential side effects (e.g., weight gain, metabolic abnormalities) associated with SGAs may suggest that the medial risks and financial costs of these drugs counterbalance the benefits of SGAs. Therefore, the aim of this study is to compare differences in weight, lipid and glucose levels, and metabolic irregularities between individuals on first and second generation antipsychotics while controlling for length of hospital stay and psychosis. It is hypothesized that patients treated with SGAs will display more weight gain and a higher prevalence of MS than individuals on FGAs. First generation antipsychotics such as perphenazine and haloperidol appear to be just as effective in treating schizophrenia as the following SGAs: quetiapine, risperidone, and ziprasidone (Lieberman et al., 2005; Rosenheck et al., 2006). Therefore, it is hypothesized that FGAs and SGAs will demonstrate similar clinical efficacy when collapsing across drug type.

Method

Research Design

Study participants were patients at Eastern State Hospital in Williamsburg, Virginia. A research proposal was submitted and approved by the hospital's Institutional Review Board (IRB). The research design was a retrospective, archival study of the

medical files of patients. A list of patients admitted to Eastern State Hospital between 1990 and 1999 and being treated with an FGA was randomly generated from admission records. An additional list of patients admitted to Eastern State Hospital between 2000 and 2006 and receiving treatment with an SGA was also created. From these lists, only current or past patients receiving treatment with an FGA or SGA for at least a six-month period were chosen for inclusion in the study. Individuals concurrently taking SGAs and FGAs were excluded from participation in the study. Demographic, clinical, and medical data were collected from patient files. Clinical and medical data were collected at two points in time in order to evaluate change in disease course across time. A pre-treatment assessment of the clinical variables was taken during the first month of admission into the hospital. The most current or discharge assessment of clinical and medical variables was recorded during December 2006. A standard de-identification process was used to protect patient confidentiality and anonymity. Participants' names, hospital record numbers, and a unique ID number were maintained on a Master Subjects Form.

Table 1 lists gender, ethnicity, and education history. Ages at last assessment ranged from 19 to 74 years (M = 44.20; Mdn = 44.00; SD = 12.09). Number of admissions to a state psychiatric facility (including current admission) ranged from 1 to 24 (M = 6.62; Mdn = 5.00; SD = 5.59). Participants length of stay in the hospital ranged from 0.21 to 13.99 years (M = 1.94; Mdn = 1.04; SD = 2.14). Table 2 lists Axis I and II psychiatric diagnoses, and Axis IV psychosocial/environmental problems. Number of Axis III medical conditions ranged from 0 to 8 (M = 2.29; Mdn = 2.00; SD = 2.03). Table 3 lists antipsychotic doses. Tables 4 and 5 list the prevalence of MS among patients receiving FGAs and SGAs.

Variables

A data collection form was developed to review each patient file. Demographic variables collected included: age, gender, ethnicity, education history of the patient, length of stay at hospital (LOS). Clinical variables were Axis I, II, III, IV, V (Global Assessment of Functioning) diagnoses from the DSM-IV-TR (American Psychological Association, 2000), Brief Psychiatric Rating Scale (BPRS) scores, and Mini Mental State Exam (MMSE) scores. The BPRS (Overall & Gorham, 1962) is a scale designed to measure the severity of psychiatric symptoms. The MMSE is used to assess cognitive status in areas of orientation, memory, and attention (Folstein, Folstein, & McHugh, 1975). Medical variables included the following: medications and their administered dosages, weight (lbs), BMI, blood pressure, and glucose and lipid levels.

Results

Statistical Measures

Frequency distributions were run on demographic variables (gender, age, ethnicity, education, and diagnoses), clinical treatment efficacy variables (Global Assessment of Functioning [GAF], BPRS total score, five BPRS scale scores, MMSE) at each time interval, and physiological variables (diagnosis of MS, BMI (body mass index), blood pressure, HDL, Triglycerides, and fasting glucose) at each time period. Measures of central tendency, dispersion, and shape were run on ordinal and interval/ratio scaled variables and continuously scaled variables.

An alpha level of 0.05 was used for all statistical analyses. Univariate and multivariate repeated measures analyses of variance were run to determine whether there was a significant change in physiological measures and clinical scores from admission to

last assessment. A separate analysis was run for diagnosis of MS, other physiological measures, and clinical scales.

Analysis of Covariance

A mixed model analysis of covariance (ANCOVA), with LOS and total number of admissions as covariates, was conducted to determine whether there was a change in mean scores on dependent measures across time period (admission, last assessment) and treatment (FGA, SGA). Violation of sphericity was corrected for by means of the Greenhouse-Geisser adjustment.

A mixed model ANCOVA was conducted on diagnosis of MS, with LOS and total number of admissions as covariates. Results indicated a significant time x treatment effect on diagnosis of MS $F(1, 77) = 4.66, p = .034$ (see Figure 1). Patients on SGAs had a greater increase in diagnosis of MS from admission ($M = .08$, $SD = .28$) to last assessment ($M = .36$, $SD = .49$) than patients on FGAs (admission, $M = .18$, $SD = .39$; last assessment, $M = .22$, $SD = .42$),

For weight, there was a significant main effect of time, $F(1, 91) = 9.57, p = .003$. Patients weighed less at admission ($M = 180.34$, $SD = 45.22$) than at last assessment ($M = 186.43$, $SD = 39.46$). There was significant time x treatment effect on weight $F(1, 91) = 7.22, p = .009$. Patients on SGAs had a greater increase in weight from admission ($M = 175.79$, $SD = 44.29$) to last assessment ($M = 188.69$, $SD = 37.91$) than patients on FGAs (admission, $M = 183.80$, $SD = 46.02$; last assessment, $M = 184.71$, $SD = 40.87$).

A 2 x 2 mixed model multivariate analysis of covariance (MANCOVA), with LOS and total number of admissions as covariates, was performed on six dependent variables: BMI, systolic and diastolic blood pressure, HDL, Triglycerides, and fasting

glucose. Independent variables were time period and treatment. With the use of Wilk's criterion, the combined DVs were not significantly affected by time or treatment. There was a nearly significant time x treatment effect on the combined dependent variables $F(6, 45) = 2.12$, $p = .069$. Univariate tests within the MANCOVA reveal a significant time x treatment effect on systolic blood pressure, $F(1, 50) = 7.40$, $p = .009$. Patients on SGAs had a greater increase in systolic blood pressure from admission ($M = 121.07$, $SD = 11.54$) to last assessment ($M = 127.48$, $SD = 13.00$) than patients on FGAs (admission, $M = 131.85$, $SD = 16.95$; last assessment, $M = 122.93$, $SD = 13.29$).

A mixed model ANCOVA on BPRS total scores, with LOS and total number of admissions as covariates, indicated a main effect of time, $F(1, 78) = 37.53$, $p = .000$. Patients had higher BPRS total scores at admission ($M = 40.98$, $SD = 10.81$) than at last assessment ($M = 32.88$, $SD = 10.14$). There was a non-significant main effect of treatment and time x treatment effect. A 2 x 2 mixed model multivariate analysis of variance (MANCOVA) was performed on the five BPRS subscales: withdrawal, cognitive dysfunction, agitation, hostile suspiciousness, and psychotic distortion. The combined dependent variables were significantly affected by time, $F(5, 74) = 9.81$, $p = .000$. Table 6 shows mean BPRS subscale scores between admission and last assessment. No main effect for treatment or time x treatment effect on the combined dependent variables was found.

Univariate mixed model ANCOVAs, with LOS and total number of admissions as covariates, were conducted on Global Assessment of Functioning (GAF) and MMSE scores. There was a significant main effect of time on GAF, $F(1, 87) = 29.63$, $p = .000$. Patients' GAF was higher at last assessment ($M = 47.55$, $SD = 14.55$) than at admission

($M = 31.62$, $SD = 11.57$). Treatment and time x treatment did not significantly affect GAF. For MMSE scores, there was significant time x treatment effect, $F(1, 30) = 6.47$, $p = .016$ (see Figure 2). Patients treated with FGAs were more likely to improve on the MMSE from admission ($M = 21.00$, $SD = 7.83$) to last assessment ($M = 27.00$, $SD = 5.61$) than those on SGAs (admission, $M = 24.89$, $SD = 4.78$; last assessment, $M = 25.79$, $SD = 5.15$). Time and treatment did not significantly affect MMSE scores.

Discussion

This study examined the prevalence of MS among schizophrenic and schizoaffective patients receiving FGAs and SGAs. Results indicated that over the course of one hospital admission, patients treated with SGAs were more likely to meet the diagnostic criteria for MS than those on FGAs. Patients receiving SGAs also displayed greater increases in weight and systolic blood pressure from first to last assessment than those being treated with FGAs. In combination, these results support previous findings that metabolic irregularities (Wu et al., 2006), weight gain (Casey, 2005), and hypertension (Meltzer, Davidson, Alexander, Glassman, & Vieweg, 2002) are side effects associated with SGA use.

Results from this study revealed that the interaction between time and treatment significantly affected diagnosis of MS but not the combined physiological risk factors for MS. These discrepancies reinforce that the diagnosis of MS is not merely an aggregate of the following physiological variables: BMI, blood pressure, HDL, triglycerides, and fasting glucose. Instead, MS is the co-occurrence of three of the following conditions: obesity, elevated blood pressure, reduced HDL, elevated triglycerides, and elevated fasting glucose. In order to meet the criteria for MS, patients did not have to evidence

abnormalities in all of the aforementioned areas (Expert Panel on Detection, 2001). Therefore, the results of the 2x2 mixed model ANCOVA are more appropriate for current study than an analysis of the combined physiological DVs. As a result, it can be concluded that there is a higher prevalence of MS among patients treated with SGAs than those receiving FGAs. This finding supports the main hypothesis of this study.

Results revealed no significant differences in Axis V or BPRS total and scale scores from first to last assessment between treatment groups. This finding suggests that SGAs and FGAs are similarly effective in reducing psychosis. The current study also found that patients treated with FGAs demonstrated greater improvements in MMSE scores over the course of one hospital admission than those on SGAs. This finding suggests that FGAs benefit cognitive functioning more than SGAs. In combination, these results indicate that SGAs are not superior to FGAs in terms of clinical efficacy.

Many researchers and clinicians have asserted the superior therapeutic efficacy of SGAs over FGAs (Marder, 2003). However, when studies have collapsed antipsychotics across drug type, as was done in the current study, results have indicated that SGAs have little or no advantage over FGAs in terms of therapeutic efficacy. Geddes et al. (2000) found that after controlling for higher than recommended FGA doses, tolerability and clinical efficacy between FGAs and SGAs was similar. In addition, SGAs showed only a slight advantage over FGAs in terms of EPS.

Methodological problems with many efficacy studies comparing FGAs to SGAs have been identified (see Rosenheck, 2005 for review). Rosenheck (2005) found that the quality of life and symptom reduction reported in many SGA efficacy studies may be inflated and give unfair advantage to SGAs. After excluding FGA doses below the

therapeutic range and FGA use without prophylactic anticholinergics, patients on low-potency FGAs were not at greater risk of non-adherence, treatment discontinuation, or developing EPS than SGAs. These findings indicate that FGAs and SGAs may have comparable treatment effectiveness.

Given the lack of support found in the current study for the superiority of SGAs on measures of therapeutic efficacy, the slightly lower risk of EPS associated with SGA use appears to be abated by the greater risk of weight gain and MS among patients receiving SGAs than those on FGAs. Metabolic syndrome is a financial burden. Given the constellation of metabolic disorders necessary for establishing a diagnosis, it is not surprising that MS is associated with an increased risk of obesity, diabetes, and cardiovascular disease (Reaven, 2002). In conjunction with the much greater drug costs of SGAs in comparison to FGAs, the annual health care costs of these conditions raise concern about the high prevalence of MS among patients receiving SGAs.

In the general population, spending per person was 37% higher in 2001 for obese persons than for those who were normal-weight (Thorpe, Florence, Howard, & Joski, 2004). Health risks associated with obesity include respiratory complications, certain cancers, liver and gall bladder disease, and hypertension (Kopelman, 2007). Because obesity both exacerbates and causes many health problems (Kopelman, 2007), obesity is a societal and economic burden. The United States Department of Health and Human Services (2001) estimated that overweight and obesity costs approximately $117 billion annually.

Diabetes mellitus and cardiovascular diseases incur some of the highest health care costs in the general population annually. The Center for Disease Control and

Prevention (2003) estimated that the annual direct cost of diabetes is approximately $92 billion in the United States. Diabetes also carries a high risk of mortality. In 2003, diabetes was the sixth leading cause of death (Hoyert, Kung, & Smith, 2005). The loss of productivity associated with diabetes' high mortality and morbidity rates contribute to the $40 billion in indirect costs of this metabolic disorder annually.

Cardiovascular disease is the leading cause of death and disability worldwide (Thom et al., 2006). Common types of cardiovascular disease include hypertension, coronary artery disease, heart failure, and stroke. Approximately 34% of all deaths in the United States in 2004 were related to cardiovascular disease. Included in the estimates of indirect costs of cardiovascular diseases is the loss of productivity associated with the high rate of morbidity and mortality of these diseases. In the general population, cardiovascular disease is the most costly disease in the United States incurring approximately $400 billion annually (Thom et al., 2006).

In addition to causing economic strain, the personal costs associated with MS are great. Metabolic syndrome adversely impacts one's quality of life (Gardner, Montgomery, & Parker, 2006). In addition, weight gain, which increases the risk of MS (Everson et al., 1998), can lead to treatment non-compliance (Awad & Vorunganti, 2004). De Hert et al. (2006) found that patients with schizophrenia who experienced recent weight gain had lower self-esteem and psychosocial adjustment than patients who had not gained weight. Recent weight gain also leads to discontinuation of treatment.

When establishing the cost-effectiveness of antipsychotics, both the financial and personal costs need to be evaluated. Second generation antipsychotics gained popularity because they carry a lower risk of EPS than FGAs. Due to the debilitating nature of EPS,

it was believed that SGAs contributed to a higher quality of life than FGAs. However, given the large economic and personal costs of MS and the higher prevalence of MS found in this study among patients receiving SGAs than those on FGAs, the cost-effectiveness of SGAs needs to be reexamined. The higher risk of MS and lack of support for the superiority of SGAs in terms of clinical efficacy found in this study suggest that the benefits of SGAs may not outweigh the side effects and financial cost of this class of antipsychotics. Further research is needed to establish the direct and indirect costs of SGAs as well as morbidity and mortality estimates of the side effects of SGAs (e.g., obesity, elevated blood pressure, and MS). In conjunction with the findings from this study, these analyses could call into question the use of SGAs as a first-line treatment for schizophrenia.

A key limitation of this research concerns the generalizability of the results. As with all quasi-experimental designs, the findings of this study should be regarded with caution. The small within group sample sizes of this study further limits the analyses of clinical efficacy between specific FGAs and SGAs. Therefore, future research should replicate this study using larger within group samples to determine the therapeutic efficacy and effectiveness of specific SGAs. Furthermore, future efforts should also be directed at determining how dose might affect the different side effect profiles of SGAs.

Table 1

Demographic Variables

	f	%
Gender		
Male	49	49.5
Female	50	50.5
Ethnicity		
African American	68	68.7
Caucasian	30	30.3
Hispanic	1	1.0
Education History		
Less than High School	7	7.5
Some High School	24	25.8
Diploma or GED	26	28.0
Some College	19	20.4
College Degree	13	14.0
Graduate Degree	4	4.3

Table 2

Primary Psychiatric Diagnoses and Psychosocial and Environmental Problems

Diagnostic Categories	*f*	%
Axis I and Axis II Diagnoses		
Schizophrenia	39	39.4
Schizoaffective Disorders	60	60.6
Substance Disorders	28	28.3
Personality Disorders	18	18.2
Mild Mental Retardation	7	7.1
Axis IV Psychosocial and Environmental Problems		
Primary Support Group	24	24.2
Social Environment	5	5.1
Educational	0	0.0
Occupational	9	9.1
Housing	23	23.2
Economic	2	2.0
Access to Health Care	37	37.4
Legal System/Crime	30	30.3
Other	1	1.0

Note. Percentage reflects percent of subjects with a diagnosis or problem in a given category. Many subjects had more than one diagnosis and problem.

Table 3

Antipsychotic Doses

Medication	*f*	%	Daily Dose (mgs) *Min*	*Max*	*M*	*Mdn*	*SD*
FGAs ($n = 56$)							
fluphenazine HCl	8	8.1	5.0	20.0	13.1	15.0	4.6
fluphenazine decanoate	13	13.1	0.2	5.4	2.7	3.6	1.7
haloperidol	19	19.2	5.0	45.0	19.3	20.0	10.2
haloperidol decanoate*	20	20.2	1.8	14.3	7.5	7.1	4.6
thioridazine	2	2.0	600.0	800.0	700.0	700.0	141.4
thiothixene	5	5.1	15.0	40.0	30.0	30.0	10.6
SGAs ($n = 43$)							
aripiprazole	2	2.0	30.0	30.0	30.0	30.0	0.0
clozapine	5	5.1	200.0	500.0	355.0	400.0	135.1
risperidone oral	12	12.1	4.0	8.0	5.7	6.0	1.4
risperidone consta	3	3.0	3.6	3.6	3.6	3.6	0.0
olanzapine	17	17.2	10.0	30.0	19.4	20.0	4.3
quetiapine	3	3.0	200.0	900.0	600.0	700.0	360.6
ziprasidone	4	4.0	160.0	160.0	160.0	160.0	0.0

Table 4

Metabolic Syndrome Among FGA Patients at Last Assessment

Metabolic Syndrome					
		Normal Range		High Risk	
	NCEP criteria	*f*	%	*f*	%
Fasting Glucose	≥ 110 mg/dl	49	87.5	7	12.5
Hypertension	≥ 130/80	33	58.9	23	41.1
Triglycerides	≥ 150 mg/dl	39	69.6	16	28.6
HDL Cholesterol	≤40 mg/dl in women	26	46.4	12	21.4
	≤50 mg/dl in men				
BMI	> 29.4 kg/m^2	36	64.3	20	35.7
MS	any 3 of the above traits	38	67.9	12	21.4

Table 5

Metabolic Syndrome Among SGA Patients at Last Assessment

Metabolic Syndrome					
		Normal Range		High Risk	
	NCEP criteria	*f*	%	*f*	%
Fasting Glucose	≥ 110 mg/dl	34	79.1	8	18.6
Hypertension	≥ 130/80	22	51.2	21	48.8
Triglycerides	≥ 150 mg/dl	27	62.8	13	30.2
HDL Cholesterol	≤40 mg/dl in women	20	46.5	18	41.9
	≤50 mg/dl in men				
BMI	> 29.4 kg/m^2	19	44.2	24	55.8
MS	any 3 of the above traits	25	58.1	14	32.6

Table 6

Mean BPRS Subscales at Admission and Last Assessment

	Admission		Last Assessment	
BPRS Subscale	*Mean*	*SD*	*Mean*	*SD*
Withdrawal	8.41	4.32	6.68	2.74
Cognitive Dysfunction	5.30	2.74	3.90	2.05
Agitation	6.26	3.25	4.79	2.15
Hostile Suspiciousness	5.45	3.06	3.99	2.08
Psychotic Distortion	6.26	2.61	4.18	2.08

Figure 1

Percentage of patients with MS

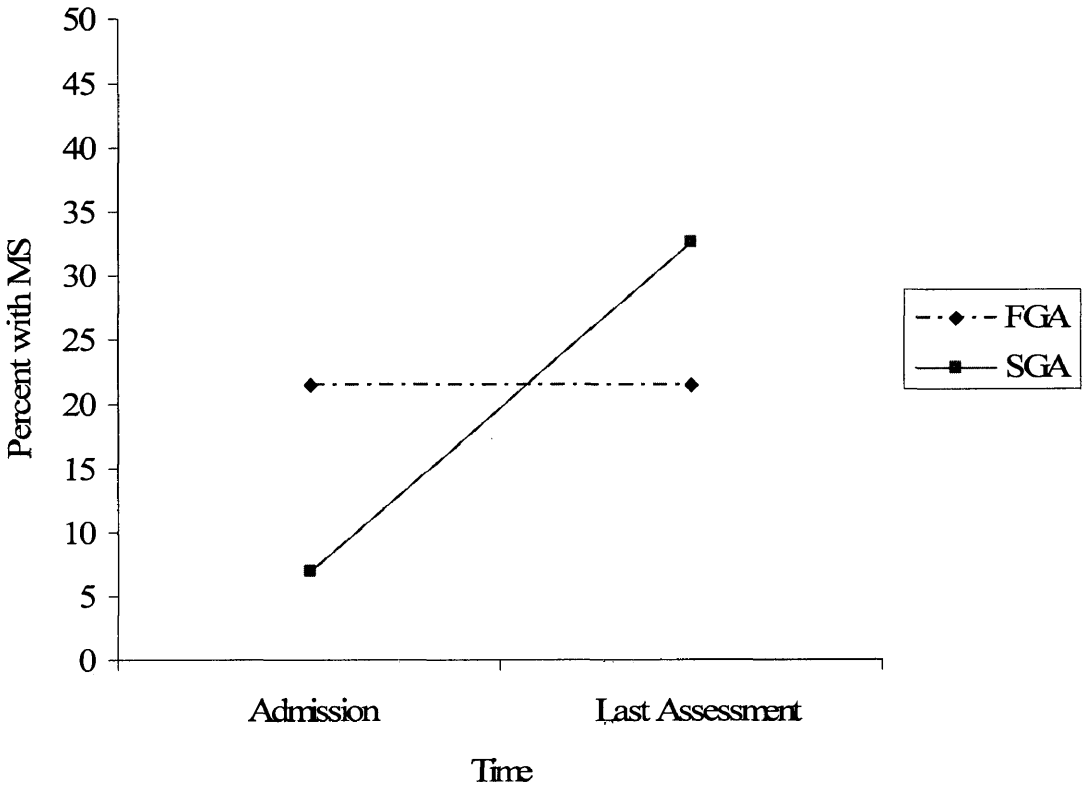
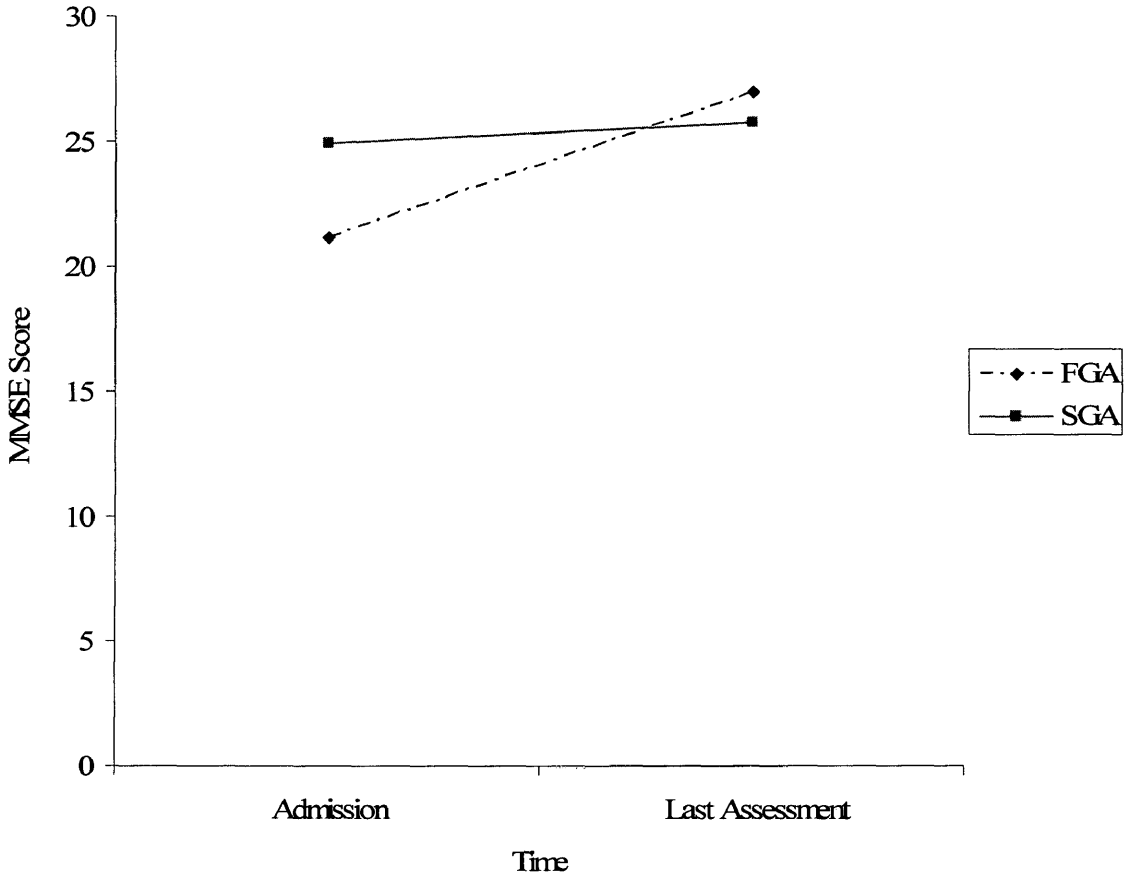


Figure 2

Estimated marginal means for MMSE scores



References

American Psychiatric Association (1997). *Practice guidelines for treatment of patients with schizophrenia.* Washington, DC: Author.

American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders –IV-TR.* Washington, DC: Author.

Andreasen, N. C. (1997). Linking mind and brain in the study of mental illnesses: A project for a scientific psychopathology. *Science, 275*, 1586-1593.

Awad, A. G., & Voruganti, L. N. P. (2004). Body weight, image and self-esteem evaluation questionnaire: Development and validation of a new scale. *Schizophrenia research, 70*, 63-67.

Ballesteros, J., González-Pinto, A., & Bulbena, A. (2000). Tardive dyskinesia associated with higher mortality in psychiatric patients: Results of a meta-analysis of seven independent studies. *Journal of Clinical Psychopharmacology, 20*, 188-194.

Baptista, T. (1999). Body weight gain induced by antipsychotic drugs: Mechanisms and management. *Acta Psychiatrica Scandinavica, 100*, 3-16.

Beard, S. M., Maciver, F., Clouth, J., & Rüther, E. (2006). A decision model to compare health care costs of olanzapine and risperidone treatment for schizophrenia in Germany. *The European Jounral of Health Economics, 7*, 165-172.

Ben-Jonathan, N. & Hnasko, R. (2001) Dopamine as a prolactin (PRL) inhibitor. *Endocrine Review, 22,* 724–763.

Bleuler, M. (1978). *The schizophrenic disorders: Long-term patient and family studies.* New Haven, CT: Yale University Press.

Bouchard R. H., Merette C., Pourcher E., Demers M. F., Villeneuve J., Roy-Gagnon M. H., et al. (2000) Longitudinal comparative study of risperidone and conventional neuroleptics for treating patients with schizophrenia. The Quebec Schizophrenia Study Group. *Journal of Clinical Psychopharmacology, 20*, 295-304.

Brown, S. (1997). Excess mortality of schizophrenia: A meta-analysis. *British Journal of Psychiatry, 171*, 502-508.

Buchanan, A. (1992). A two-year prospective study of treatment compliance in patients with schizophrenia. *Psychological Medicine, 22,* 787–797.

Burton, S. (2006). Symptom domains of schizophrenia: The role of atypical antipsychotic agents. *Journal of Psychopharmacology, 20*, 6-19.

Cahn, W., Hulshoff, H. E., Lems, E. B. T. E., van Haren, N. E. M., Schnack, H. G., van der Linden,Jeroen A., et al. (2002). Brain volume changes in first-episode schizophrenia: A 1-year follow up study. *Archives of General Psychiatry, 59*, 1002-1010.

Carney, C. P., Jones, L., & Woolson, R. F. (2006). Medical comorbidity in women and men with schizophrenia: A population-based controlled study. *Journal of General Internal Medicine, 21*, 1207-1208.

Casey, E. (1998). Effects of clozapine therapy in schizophrenic individuals at risk for tardive dyskinesia. *Journal of Clinical Psychiatry, 59,* 31–37.

Centers for Disease Control and Prevention (2003). National diabetes fact sheet: General information and national estimates on diabetes in the United States, 2002. U.S. Department of Health and Human Services. Retrieved April 12, 2007 from http://www.diabetes.org.

Correll, C. U., Leucht, S., & Kane, J. M. (2004). Lower risk for tardive dyskinesia associated with second-generation antipsychotics: A systematic review of 1-year studies. *American Journal of Psychiatry, 161*, 414-425.

Crook, J. M., Tomaskovic-Crook, E., Copolov, D. L., & Dean, B. (2001). Low muscarinic receptor binding in prefrontal cortex from subjects with schizophrenia: A study of brodmann's areas 8, 9, 10, and 46 and the effects of neuroleptic drug treatment. *American Journal of Psychiatry, 158*, 918-925.

Csernansky, J. G., & Schuchart, E. K. (2002). Relapse and rehospitalisation rates in patients with schizophrenia: Effects of second generation antipsychotics. *CNS Drugs, 16*, 473-484.

De Hert, M., Peuskens, B., van Winkel, R., Kalnicka, D., Hanssens, L., Van Eyck, D., et al. (2006). Body weight and self-esteem in patients with schizophrenia evaluated with B-WISE. *Schizophrenia Research, 88*, 222-226.

Dixon, L., Postrado, L., Delahanty, J., Fischer, P. J., & Lehman, A. (1999). The association of medical comorbidity in schizophrenia with poor physical and mental health. *Journal of Nervous and Mental Disease, 187*, 496-502.

Dixon, L., Weiden, P., Delahanty, J., Goldberg, R., Postrado, L., Lucksted, A., et al. (2000). Prevalence and correlates of diabetes in national schizophrenia samples. *Schizophrenia bulletin, 26*, 903-912.

Everson, S., Goldberg, D. E., Helmrich, S., Lakka, T., Lynch, J., Kaplan, G., et al. (1998). Weight gain and the risk of developing insulin resistance syndromes. *Diabetes Care, 21*, 1637-1643.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. (2001). Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *Journal of the American Medical Association, 285*, 2486-2497.

Farde, L., Mack, R. J., Nyberg, S., & Halldin, C. (1997). D-sub-2 occupancy, extrapyramidal side effects and antipsychotic drug treatment: A pilot study with sertindole in healthy subjects. *International Clinical Psychopharmacology, 12*, S3-S7.

Gardner A. W., Montgomery P. S., Parker, D. E. (2006). Metabolic syndrome impairs physical function, health-related quality of life, and peripheral circulation in patients with intermittent claudication. *Journal of Vascular Surgery, 43*, 1191-1197.

Geddes, J., Freemantle, N., Harrison, P., & Bebbington, P. (2000). Atypical antipsychotics in the treatment of schizophrenia: Systematic overview and meta-regression analysis. *British Medical Journal, 321*, 1371-1376.

Gerlach, J. (1999). The continuing problem of extrapyramidal symptoms: Strategies for avoidance and effective treatment. *Journal of Clinical Psychiatry, 60*, 20-24.

Gerlach, J. (2002). Improving outcome in schizophrenia: The potential importance of EPS and neuroleptic dysphoria. *Annals of Clinical Psychiatry, 14*, 47-57.

Goldman, L. S. (1999). Medical illness in patients with schizophrenia. *Journal of Clinical Psychiatry, 60*, 10-15.

Haro, J. M., & Salvador-Carulla, L. (2006). The SOHO (schizophrenia outpatient health outcome) study: Implications for the treatment of schizophrenia. *CNS Drugs, 20*, 293-301.

Horacek, J., Bubenikova-Valesova, V., Kopecek, M., Palenicek, T., Dockery, C., Mohr, P., et al. (2006). Mechanism of action of atypical antipsychotic drugs and the neurobiology of schizophrenia. *CNS Drugs, 20*, 389-409.

Hoyert, D. L., Kung, H. C., & Smith, B. L. (2005). Preliminary data for 2003. *National Vital Statistics Reports, 53*. Retrieved April 12, 2007 from http://www.cdc.gov/nchs/data/nvsr/nvsr53/nvsr53_15.pdf.

Ikebuchi, E., Nakagome, K., & Takahashi, N. (1999). How do early stages of information processing influence social skills in patients with schizophrenia? *Schizophrenia research, 35*, 255-262.

Javitt, D. C., & Laruelle, M. (2006). Neurochemical theories. In J. A. Lieberman, T. S. Stroup & D. O. Perkins (Eds.), *The American Psychiatric Publishing Textbook of Schizophrenia.* (pp. 85-116) American Psychiatric Publishing.

Jin, H., Meyer, J. M., & Jeste, D. V. (2004). Atypical antipsychotics and glucose dysregulation: A systematic review. *Schizophrenia Research, 71*, 195-212.

Kane, J. M. (2001). Extrapyramidal side effects are unacceptable. *European Neuropsychopharmacology, 11*, S397-S403.

Kapur, S., & Mamo, D. (2003). Half a century of antipsychotics and still a central role for dopamine D-sub-2 receptors. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 27*, 1081-1090.

Kasper, S., & Resinger, E. (2003). Cognitive effects and antipsychotic treatment. *Psychoneuroendocrinology, 28*, 27-38.

Kopelman, P. (2007). Health risks associated with overweight and obesity. *Obesity Reviews, 8,* 13-17.

Kotrla, K. J., & Weinberger, D. R. (1995). Brain imaging in schizophrenia. *Annual Review of Medicine, 46*, 113-122.

Krausz, M., Moritz, S. H., Naber, D., Lambert, M., & Andresen, B. (1999). Neuroleptic-induced extrapyramidal symptoms are accompanied by cognitive dysfunction in schizophrenia. *European Psychiatry, 14*, 84-88.

Lacroix, L. P., Hows, M. E. P., Shah, A. J., Hagan, J. J., & Heidbreder, C. A. (2003). Selective antagonism at dopamine D-sub-3 receptors enhances monoaminergic and cholinergic neurotransmission in the rat anterior cingulate cortex. *Neuropsychopharmacology, 28*, 839-849.

Lieberman, J. A., Stroup, T. S., McEvoy, J. P., Swartz, M. S., Rosenheck, R. A., Perkins, D. O., et al. (2005). Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *New England Journal of Medicine, 353*, 1209-1223.

Mamo, D., Kapur, S., Shammi, C. M., Papatheodorou, G., Mann, S., Therrien, F., et al. (2004). A PET study of dopamine D-sub-2 and serotonin 5-HT-sub-2 receptor occupancy in patients with schizophrenia treated with therapeutic doses of ziprasidone. *American Journal of Psychiatry, 161*, 818-825.

Marder, S. R. (2003). Evicence for using atypical antipsychotics in psychosis. *Journal of Clinical Psychiatry, 5*, 22-26.

Marder, S. R., Essock, S. M., Miller, A. L., Buchanan, R. W., Casey, D. E., Davis, J. M., et al. (2004). Physical health monitoring of patients with schizophrenia. *American Journal of Psychiatry, 161*, 1334-1349.

Meltzer, H. Y., Davidson, M., Glassman, A. H., & Vieweg, V. R. (2002). Assessing cardiovascular risks versus clinical benefits of atypical antipsychotic drug treatment. *Journal of Clinical Psychiatry, 63*, 25-29.

Meyer, J. M. (2003). Cardiovascular illness and hyperlipidemia in patients with schizophrenia. In J. M. Meyer & H. Nasrallah (Eds.), *Medical Illness and Schizophrenia. American Psychiatric Press* (pp. 59–89). Washington, DC: American Psychiatric Press.

Mukherjee, S. (1982). Tardive dyskinesia in psychiatric outpatients: A study of prevalence and association with demographic, clinical, and drug history variables. *Archives of General Psychiatry, 39*, 466-469.

National Institute of Mental Health (2005). *Schizophrenia.* Retrieved April 17, 2006 from http://www.nimh.nih.gov/publicat/schizoph.cfm.

Newcomer, J. W., Haupt, D. W., Fucetola, R., Melson, A. K., Schweiger, J. A., Cooper, B. P., et al. (2002). Abnormalities in glucose regulation during antipsychotic treatment of schizophrenia. *Archives of General Psychiatry, 59*, 337-345.

Nichols, G. A. & Brown, J. B. (2005). Higher medical care costs accompany impaired fasting glucose. *Diabetes Care, 28*, 2223-2229.

Peroutka, S., & Snyder, S. H. (1980). Relationship of neuroleptic drug effects at brain dopamine, serotonin, !a-adrenergic, and histamine receptors to clinical potency. *American Journal of Psychiatry, 137*, 1518-1522.

Reaven, G. (2002). Metabolic syndrome: Pathophysiology and implications for management of cardiovascular disease. *Circulation, 106,* 286-288.

Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., et al. (1990). Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area (ECA) Study. *Journal of the American Medical Association, 264*, 2511–2518.

Rice, D. P. (1999). The economic impact of schizophrenia. *Journal of Clinical Psychiatry, 60*, 4-6.

Rosenheck, R. A. (2005). Effectiveness versus efficacy of second-generation antipsychotics: Haloperidol without anticholinergics as a comparator. *Psychiatric Services, 56*, 85-92.

Rosenheck, R. A., Leslie, D. L., Sindelar, J., Miller, E. A., Lin, H., Stroup, T. S., et al. (2006). Cost-effectiveness of second-generation antipsychotics and perphenazine in a randomized trial of treatment for chronic schizophrenia. *The American Journal of Psychiatry, 163*, 2080-2089.

Sayers, A. C., Burki, H. R., Ruch, W., & Asper, H. (1976). Anticholinergic properties of antipsychotic drugs and their relation to extrapyramidal side-effects. *Psychopharmacology, 51*, 15-22.

Shean, G. D. (2004). *Understanding and treating schizophrenia: Contemporary research, theory, and practice.* Haworth Press.

Smith, T. E., Hull, J. W., Romanelli, S., Fertuck, E., & Weiss, K. A. (1999). Symptoms and neurocognition as rate limiters in skills training for psychotic patients. *American Journal of Psychiatry, 156*, 1817-1818.

Soares, K. V. S., & McGrath, J. J. (1999). The treatment of tardive dyskinesia--a systematic review and meta-analysis. *Schizophrenia Research, 39*, 1-16.

Sokal, J., Messias, E., Dickerson, F. B., Kreyenbuhl, J., Brown, C. H., Goldberg, R. W., et al. (2004). Comorbidity of medical illnesses among adults with serious mental illness who are receiving community psychiatric services. *Journal of Nervous and Mental Disease, 192*, 421-427.

Strejilevich, S. A., Palatnik, A., Avila, R., Bustin, J., Cassone, J., Figueroa, S., et al. (2005). Lack of extrapyramidal side effects predicts quality of life in outpatients treated with clozapine or with typical antipsychotics. *Psychiatry Research, 133*, 277-280.

Synder, S. H., Greenberg, D., & Yamumura, H. I. (1974). Antischizophrenic drugs: Affinity for muscarinic cholinergic receptor sites in the brain predicts extrapyramidal effects. *Journal of Psychiatric Research, 11*, 91-95.

Tarsy, D., & Baldessarini, R. J. (2006). Epidemiology of tardive dyskinesia: Is risk declining with modern antipsychotics. *Movement Disorders, 21*, 589–98.

Thom T., Haase N., Rosamond W., Howard V. J., Rumsfeld J., Manolio T., Zheng Z. J., et al. (2006). Heart disease and stroke statistics—2006 update: A report from the

American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation 113*, 85–151.

Thorpe, K. E., Florence, C. S., Howard, D. H., & Joski, P. (2004). The impact of obesity on rising medical spending. *Health Affairs*, W5/317-W5/325. Retrieved April 12, 2007 from http://content.healthaffairs.org/cgi/reprint/hlthaff.w4.480v1.pdf.

Toomey, R., Seidman, L. J., Lyons, M. J., Faraone, S. V., & Tsuang, M. T. (1999). Poor perception of nonverbal social-emotional cues in relatives of schizophrenic patients. *Schizophrenia Research, 40*, 121-130.

U.S. Department of Health and Human Services. (2001). The Surgeon's General's calls to action to prevent and decrease overweight and obesity. Retrieved April 12, 2007 from http://www.surgeongeneral.gov/topics/obesity/

Velligan, D. I., Mahurin, R. K., Diamond, P. L., Hazleton, B. C., Eckert, S. L., & Miller, A. L. (1997). The functional significance of symptomatology and cognitive function in schizophrenia. *Schizophrenia Research, 25*, 21-31.

Weiden, P. J. (2007). EPS profiles: The atypical antipsychotics are not all the same. *Journal of Psychiatric Practice, 13*, 13-24.

Wiser, A. K., Andreasen, N. C., O'Leary, D. S., Watkins, G. L., Ponto, L. L. B., & Hichwa, R. D. (1998). Dysfunctional cortico-cerebellar circuits cause 'cognitive dysmetria' in schizophrenia. *Neuroreport, 9*, 1895-1899.

Worrel, J. A., Marken, P. A., Beckman, S. B., & Ruehter, V. (2000). Atypical antipsychotic agents: A critical review. *American Journal of Health Systems and Pharmacology, 52*, 238-255.

Wu, E. Q., Birnbaum, H. G., Shi, L., Ball, D. E., Kessler, R. C., Moulis, M., et al. (2005). The economic burden of schizophrenia in the united states in 2002. *Journal of Clinical Psychiatry, 66*, 1122-1129.

Wu, R., Zhao, J., Liu, Z., Zhai, J., Guo, X., Guo, W., et al. (2006). Effects of typical and atypical antipsychotics on glucose-insulin homeostasis and lipid metabolism in first-episode schizophrenia. *Psychopharmacology, 186*, 572-578.

Zhang, W., & Bymaster, F. P. (1999). The in vivo effects of olanzapine and other antipsychotic agents on receptor occupancy and antagonism of dopamine D-sub-1, D-sub-2, D-sub-3, 5HT-sub(2A) and muscarinic receptors. *Psychopharmacology, 141*, 267-278.

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